AnnMarie O'Donoghue was born in Dublin (Ireland) in 1973. She studied for her BSc degree (Chemistry) in University College Dublin. She remained at the same institution for her PhD studies in physical organic chemistry under the supervision of Professor Rory More O'Ferrall. Her PhD was awarded in November 1999 for her research on the formation and reactions of reactive carbocation intermediates. In 1999, she was awarded a Fulbright Fellowship to pursue postdoctoral studies in the research group of Professor John Richard in the University at Buffalo, the State University of New York (USA). There she worked on the dynamics of the proton transfer reactions of triosephosphate isomerase. She returned to University College Dublin for a brief period in 2002 as a short-term Lecturer in Organic Chemistry. In 2003, she was awarded a Marie Curie Fellowship for postdoctoral studies on the directed evolution of proteins with Dr Florian Hollfelder in the Department of Biochemistry, University of Cambridge (UK). From 2004-2005, she again returned to University College Dublin as a Lecturer in Organic Chemistry. In 2005 she moved to a Lectureship in Physical Organic Chemistry in the Department of Chemistry, Durham University (UK). Apart from a career break in 2008-2009 due to the birth of twins, she has since remained in Durham University as an independent researcher and was promoted to Senior Lecturer in 2012. Her research focuses on mechanistic studies of organic and biological transformations with a special interest in organocatalysis.

What is the focus of your current research activity?

The focus of my current research is the study of organic and biological reaction mechanisms. Through understanding the strategies underpinning catalysis, we aim to inform the design of improved catalyst systems. We use a physical organic chemistry approach towards deciphering reaction mechanisms based on organic synthesis, reaction kinetics, isotopic labelling and structure-activity studies.

When did you get interested in synthesis?

From early in my undergraduate studies, I enjoyed making molecules and it became clear that synthesis underpins all areas of organic chemistry. Physical organic chemistry has allowed me to combine my interest in

synthetic chemistry with the application of physical methods for the determination of reaction mechanism.

What do you think about the modern role and perspectives of organic synthesis?

In the last few decades, there have been huge developments in synthetic organic chemistry. There now exist successful methodologies for many challenging organic transformations and efficient catalyst systems for numerous synthetic processes. Given these many significant advances, the task of identifying further new organic synthetic chemistry and catalyst systems is difficult. I believe that further developments in synthetic chemistry, particularly in catalysis, will hinge upon a deeper fundamental understanding of underlying mechanisms and modes of action. Research in physical organic chemistry must keep in step with developments in synthetic chemistry.

Your research group is active at the interface of organic and biological chemistry, with a focus on catalysis. Could you tell us more about your research and its aims?

Despite the large increase in the application of small molecule organocatalysts there have been few detailed studies of catalytic mechanism. We are currently studying the mechanisms of three key classes of organocatalyst: N-heterocyclic carbene, dimethylaminopyridine-derived and Brønsted acid/base organocatalysts. Organocatalyst systems often require higher catalysts loadings than metal-based analogues and there is significant scope for mechanism-guided improvement. Our interests in enzyme catalysis partly focus on understanding how enzymes achieve such remarkable product specificities. Significant attention has been devoted to the origin of the extraordinary rate accelerations achieved by enzymes, however, much less focus has been dedicated to the equally important factor of how enzymes suppress competing side reactions. Originating from my postdoctoral studies, we are also probing enzymatic catalysis of proton transfer processes that are ubiquitous to many chemical transformations. The main tool that we employ in the study of enzymatic mechanism is the kinetic analysis of chemically designed ‘synthetic’ mutant substrates. As well as providing general insight into enzymatic catalysis, we also hope to translate our research into the design of small molecule catalyst systems.

What is your most important scientific achievement to date and why?

As part of a project investigating the mechanisms of nucleophilic organocatalysis by carbenes, we have recently studied the proton transfer reactions of a large series of N-heterocyclic carbenes (NHCs). Typically in organocatalytic applications of NHCs, the carbene is generated *in situ* by deprotonation of the conjugate acid azolium precursor by a suitable base. We have studied over 50 different NHCs, comprising several carbene classes, and have determined both kinetic acidities towards deprotonation by a common base and also pK_a values in water. Surprisingly, the kinetic acidities vary by over 10^{13}-fold and the pK_a values by 13 units within the series. These studies have enabled the influences of a range of structural features on fundamental NHC acid-base properties to be probed including the effects of ring heteroatom, ring size, internal NCN angle, the electronic and steric nature of substituents, and linker size in *bis*-carbene systems.

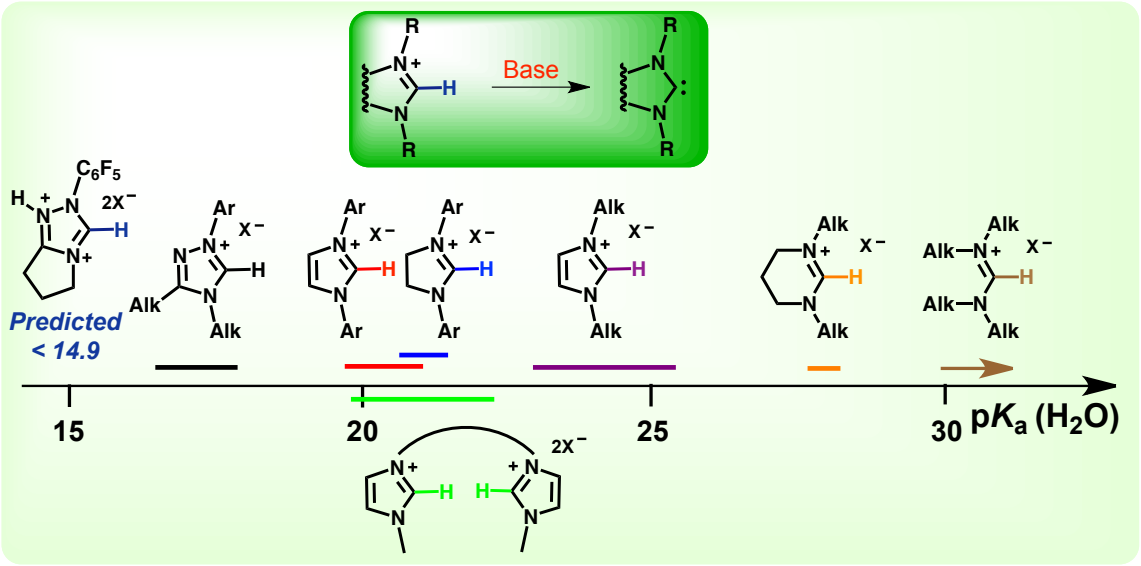

Figure 1 *pK_a scale for the conjugate acids of N-heterocyclic carbenes in water.*